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09/310,667	05/12/1999	DAVID J. ECKER	IBIS-0012	9164

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EXAMINER
LU, FRANK WEI MIN

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 01/15/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/310,667	ECKER ET AL.	
	Examiner	Art Unit	
	Frank W Lu	1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 October 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *26-29, 35-41, and 43-67* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26-29, 35-41, and 43-67* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☒ The proposed drawing correction filed on *21 October 2002* is: a)☐ approved b)☒ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15)☐ Notice of References Cited (PTO-892)
16)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18)☐ Interview Summary (PTO-413) Paper No(s). _____ .
19)☐ Notice of Informal Patent Application (PTO-152)
20)☐ Other: .

Response to Amendment

1. Applicant's response to the office action filed on October 21, 2002 has been entered as Paper No: 25. The claims pending in this application are claims 27-29, 35-41, and 43-67. Rejection and/ or objection not reiterated from the previous office action are hereby withdrawn.

Specification

2. The substitute specification filed on October 21, 2002 has been entered as Paper No: 26.

Drawings

3. The corrected drawings submitted on October 21, 2002 have been disapproved because they introduce new matter into the drawings. 37 CFR 1.121(a)(6) states that no amendment may introduce new matter into the disclosure of an application. The added or deleted materials in Figures 4 and 5A which are not supported by the original disclosure is as follows:

(1) in the corrected Figure 4, "Annotations-Relational Database" was replaced with "parsed Annotations". The meanings of these phrases are different.

(3) in the corrected Figure 5A ,"Is CurrWin≥maxWin size?" was replaced with "CurrWin≥maxWin ". The meanings of these phrases are different.

Applicant is required to cancel these new matters in the reply to this Office Action.

Claim Rejections - 35 U.S.C. § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 35-41, and 43-67 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Although the specification describes iron response element and 3' untranslated region of the histone mRNA (see specification, pages 32-38), the specification does not adequately describe that : (1) an oligonucleotide comprising a molecular interaction site that is present in the RNA does not comprise the iron response element in claims 35-41 and 43-51; and (2) an oligonucleotide comprising a molecular interaction site that is present in the RNA does not comprise the iron response element or the 3' untranslated region of the histone mRNA in claims 52-67. MPEP 2163.06 states that "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. *In re Rasmussen*, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)." In view of the embodiments adequately description in the specification, the subject application does not reasonably convey to one skilled in the art that applicant was in possession of the full scopes of products encompass in the claims at the time of the application was filled. Therefore, the written description requirement has not been satisfied.

In support of this position, attention is directed to the decision of *Vas-Cath inc. V. Mahurkar* 19 USPQ2d 1111 (CAFC, 1991):

This court in *Wilder* (and the CCPA before it) clearly recognized, and we hereby reaffirm, that 35 U.S.C. 112, first paragraph, requires a "written description of the invention" which is separate and distinct from the enablement requirement. The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the "applicant must also convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the "written description" inquiry, *whatever is now claimed.*

Response to Arguments

In page 4 bridging to page 5, first paragraph of applicant's remarks, applicant argued that: (1) "a person of ordinary skill in the art would have been able to tell that the inventors had complete possession of the claimed invention" since "the art-skilled would be able to determine if an oligonucleotide contained an iron responsive element or the 3'-untranslated region of the histone mRNA."; and (2) "it is established law that limitations appearing in the claims need not be literally recited in the specification." since "[T]he issue is not whether words used in the claims are present in the specification but, rather, whether the concept expressed by the words is present.".

These arguments have been fully considered but they are not persuasive toward the withdrawal of the rejection. First, although the specification describes 3' untranslated region of the histone mRNA (see specification, pages 37 and 38), the specification does not adequately describe that: (1) an oligonucleotide comprising a molecular interaction site that is present in the RNA does not comprise the iron response element in claims 35-41 and 43-51; and (2) an oligonucleotide comprising a molecular interaction site that is present in the RNA does not comprise the iron response element or the 3' untranslated region of the histone mRNA in claims 52-67. In view of the embodiments adequately description in the specification, the subject application does not reasonably convey to one skilled in the art that applicant was in possession of

the full scopes of products encompass in the claims at the time of the application was filled. On other word, one skilled in the art will not recognize "applicant's claimed invention did not include the 3' untranslated region of the histone mRNA". The examiner's rejection was not based on "the art-skilled would be able to determine if an oligonucleotide contained an iron responsive element or the 3'-untranslated region of the histone mRNA". Second, although the examiner agreed with applicant that "limitations appearing in the claims need not be literally recited in the specification", applicant did not indicate, in the specification, where described an oligonucleotide comprising a molecular interaction site that was present in the RNA did not comprise the iron response element and an oligonucleotide comprising a molecular interaction site that was present in the RNA did not comprise the iron response element or the 3' untranslated region of the histone mRNA.

Claim Rejections - 35 U.S.C. § 102/103

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 35-40, 43-57, and 59-67 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Manzella *et al.*, (J. Biol. Chem., 267, 7077-7082, 1992).

Manzella *et al.*, teach binding of a specific protein(s) to a conserved region of the ornithine decarboxylase mRNA 5'-untranslated region. In this study, one or more cellular protein(s) (ornithine decarboxylase mRNA 5'-UTR binding protein (ODCBP)), that bound specifically to a conserved region of the 5'- untranslated region (5'-UTR) of rat ornithine decarboxylase (ODC) mRNA as recited in claims 35, 40, 51, 52, 57, and 67 was identified using a RNA gel retardation assay. A similar binding activities was found in cytoplasmic extracts from a variety of animal cells and tissues such as human tumor cells, mouse and rat fibroblast, and cow brain as recited in claims 35, 39, 51, 52, 56, and 67 (see pages 7077-7080). Note that: (1) although Manzella *et al.*, did not directly disclose that modulation of the expression of ornithine decarboxylase mRNA by binding of a protein cytoplasmic extracts to ornithine decarboxylase mRNA 5'-UTR as recited in claims 35, 51, 52, and 67, this limitation was considered to be an

inherent property of ornithine decarboxylase mRNA since there was no structural difference between ornithine decarboxylase mRNA and claimed oligonucleotde recited in claims 35, 51, 52, and 67 and it was known that the ornithine decarboxylase mRNA 5'-UTR regulated the expression of ornithine decarboxylase mRNA (see right column in page 7077); and (2) although the molecular interaction site taught by Manzella *et al.*, was not identified by the method recited in claims 35-38, 43-55, and 59-67, it is well established that even though product-by process claims are limited by and defined by the process, the determination of the patentability of the product is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process."*In re Thorpe*, 227 USPQ 964, 966 (Fed. Cir. 1985).

Response to Arguments

In page 5, third paragraph bridging to page 6, last paragraph of applicant's remarks, applicant argued that: (1) "The Manzella reference does not teach or suggest a molecular interaction site that modulates the expression of RNA" since "[M]anzella discloses examples of proteins binding to an oligonucleotide, but does not disclose that the binding of these proteins to the oligonucleotide that modulates the expression of the mRNA."; and (2) "applicant's claims are not 'product-by-process' claims" since "[A]pplicants have described their claimed invention recited in claims 35-41 and 43-51 primarily in terms of structure or physical characteristics and not by the process by which the invention is made.".

These arguments have been fully considered but they are not persuasive toward the withdrawal of the rejection. First, Manzella *et al.,* did disclose that the binding of these proteins to the oligonucleotide that modulates the expression of the mRNA since it was known that the ornithine decarboxylase mRNA 5'-UTR regulated the expression of ornithine decarboxylase mRNA (see right column in page 7077). Second, the examiner agreed with applicant that claimed product recited in claims 35-41 and 43-51 with some structure or physical characteristics. However, since a molecular interaction site in an oligonucleotide was identified by a method recited in claims 35-41 and 43-51, the examiner still considered the claimed invention was a product-by process claims. Note that the determination of the patentability of the product is based on the product itself. The patentability of a product does not depend on its method of production (note that claims 36-41, 43-50, 53-57, and 59-66 are method claims and are dependent on the methods recited in claims 38 and 52). If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process."*In re Thorpe*, 227 USPQ 964, 966 (Fed. Cir. 1985).

13. Claims 27-29, 35-38, 41, 43-55, and 58-67 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Garcia *et al.,* (J. Mol. Biol. 254, 247-259, 1995) in light of Molecule Cell Biology (second Edition, edited by Darnell et al., pages 99-101, 1990) and Textbook of Biochemistry with clinical correlations (third edition, Edited by Thomas Devlin, 1992, page 739).

Garcia *et al.,* teach solution structure of the ribosome-binding domain of *E. coli* translation initiation factor IF3. As acknowledged by Garcia, in prokaryotic organisms, the first step in the initiation of protein translation was the binding of the 3' region of the 16S ribosomal RNA to the complementary 'Shine & Dalgarno' sequence located a few bases upstream to the start codon of mRNA. This ensured a pre-positioning of the 30S ribosome (see page 247). Note that: (1) although Garcia *et al.,* did not directly show to this interaction was specific for prokaryotic organisms as described claims 27, 41, and 58, this limitation was considered as inherent to the reference taught by Garcia *et al.*, since it was known that eukaryotes did not utilize this mRNA-rRNA base pair mechanism and 'Shine & Dalgarno' sequence was only found in prokaryotic organisms, not in eukaryotic RNA and human RNA as recited in claims 28 and 29 and the interaction between IF3 and 30S subunit of the ribosome was specific for prokaryotic organisms (see right column in page 248; Molecule Cell Biology, second Edition, edited by Darnell et al., pages 99-101; Textbook of Biochemistry with clinical correlations, third edition, Edited by Thomas Devlin, page 739); (2) "Shine & Dalgarno" sequence in mRNA that could bind to 16S RNA to could be considered as a molecular interaction site as recited in claims 35, 51, 52, and 67; (3) the binding of the 3' region of the 16S ribosomal RNA to the complementary 'Shine & Dalgarno' sequence located a few bases upstream to the start codon of mRNA was considered to modulate mRNA expression as recited in claims 27, 35, 51, 52, and 67; and (4) although the molecular interaction site taught by Garcia *et al., et al.,* was not identified by the methods recited in claims 35-38, 43-55, and 59-67, it is well established that even though product-by process claims are limited by and defined by the process, the determination of the patentability of the

product is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process."*In re Thorpe*, 227 USPQ 964, 966 (Fed. Cir. 1985).

Response to Arguments

In page 7 bridging to page 9, second paragraph of applicant's remarks, applicant argued that: (1) "the Garcia reference fails to teach or suggest an oligonucleotide, let alone an oligonucleotide that comprises a molecular interaction site, as recited in claims 27 and 35 " since " the 16S RNA molecule that is relied on for the instant rejection is not an oligonucleotide, as called for by the claims."; (2) "[T]he Garcia reference further fails to teach or suggest that the molecular interaction site of the 16S RNA is present in 'least one additional prokaryotic RNA,' as recited in the claims." ; and (3) "the Office Action fails to provide a reason as to why one of ordinary skill in the art would have been led to modify the ribosomal subunit of the Garcia reference to arrive at the oligonucleotide of claimed invention.".

These arguments have been fully considered but they are not persuasive toward the withdrawal of the rejection. First, Garcia *et al.,* did teach an oligonucleotide that comprises a molecular interaction site since a nucleotide sequence comprising Shine & Dalgarno sequence in mRNA or a nucleotide sequence comprising its complementary sequence in 16 S RNA was considered as an oligonucleotide comprising a molecular interaction site that was present in the RNA of a selected organism as recited in claims 27 and 35. Applicant did not indicate why nucleotide sequence comprising Shine & Dalgarno sequence in mRNA or a nucleotide sequence

comprising its complementary sequence in 16 S RNA could not be called as a oligonucleotide. Second, although Garcia reference did not directly show that the molecular interaction site of the 16S RNA or mRNA was present in "least one additional prokaryotic RNA", it was known that all bacteria mRNA had Shine & Dalgarno sequence and small RNA as 16S RNA in bacteria had complementary sequence of Shine & Dalgarno sequence (see Molecule Cell Biology, second Edition, edited by Darnell et al., page 99, 1990). Third, the Office Action did not need to "provide a reason as to why one of ordinary skill in the art would have been led to modify the ribosomal subunit of the Garcia reference to arrive at the oligonucleotide of claimed invention." since Garcia *et al.,* in light of the textbook of Molecule Cell Biology and Textbook of Biochemistry with clinical correlations have taught claimed invention. Note that the textbook of Molecule Cell Biology and Textbook of Biochemistry with clinical correlations were used to support the reference of Garcia *et al.,* since Garcia *et al.,* did not detailed describe the effect of Shine & Dalgarno sequence.

Conclusion

14. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

15. No claim is allowed.

16. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is either (703) 308-4242 or (703)305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (703) 305-1270. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703) 308-1152.

Any inquiry of a general nature or relating to the status of this application should be directed to the patent Analyst of the Art Unit, Ms. Chantae Dessau, whose telephone number is (703) 605-1237.

Frank Lu
January 2, 2003

Ethan Whisenant, Ph.D.
Primary Examiner (FSA)